

**I. AMENDMENTS**

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**IA. AMENDMENTS TO THE SUBSTITUTE SPECIFICATION**

TECH CENTER 1600/2300

Please amend the paragraph on page 10, beginning on line 1 (i.e., paragraph 0051) of the Substitute Specification, as follows:


C1 A compound of the invention is a peptide comprising from 10 to 50 amino acids. The amino acids are preferably one of the twenty naturally occurring L-amino acids. However, D-amino acids may be present as may amino acid analogs. A sequence of the invention will comprise an integrin binding motif such as RGD sequence in either the L- or D- form but preferably in the L-conformation. The peptide of the invention can be amidated or non-amidated on its C-terminus, or carboxylated or non-carboxylated on its N-terminus. The peptide of the invention may or may not contain a glycosaminoglycan binding motif such as SGD~~G~~ (SEQ ID NO:01) sequence in L- or D-isomer form. A compound of the invention is still further characterized by biological activity i.e. it enhances skeletal growth as well as the growth or recruiting of osteoblast or odontoblast cells on surface of the new skeletal growth.

Please amend the paragraph on page 10, beginning on line 12 (i.e., paragraph 0052) of the Substitute Specification, as follows:

C2 Specific examples of peptides of the invention comprise seven to forty-seven amino acids on either side of the RGD sequence of the naturally occurring sequence of matrix extracellular phosphoglycoprotein. Thus, examples of peptides of the invention comprising sequences taken from the following sequence and including the RGD sequence shown in bold:


DSQAQKSPVKSKSTHRIQHNIDYLNKHLKLVKKIPSDFE~~GS~~GYTDLQ**ERGD**NDISPFSGDG  
QPFKDIPGKGEATGPDLEGKDITGFAGPSEAESTHL (SEQ ID NO:02).

Please amend the paragraph on page 10, beginning on line 19 (i.e., paragraph 0053) of the Substitute Specification, as follows:

 Specific examples of peptides of the invention which comprise the RGD sequence as the terminal sequence include the following:


AQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFEGSGYTDLQERGD (SEQ ID NO:03)  
RGDAQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFEGSGYTDLQE (SEQ ID NO:04)  
DSQAQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFEGSGYTDRGD (SEQ ID NO:05)  
RGDSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFEGSGYTDLQE (SEQ ID NO:06)  
DSQAQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFEGSGRGD (SEQ ID NO:07)  
RGDTHRIQHNIDYLNKHLKSVKKIPSDFEGSGYTDLQE (SEQ ID NO:08)  
DSQAQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSDFERGD (SEQ ID NO:09)  
RGDLKHLKSVKKIPSDFEGSGYTDLQE (SEQ ID NO:10)  
DSQAQKSPVKSSTHRIQHNIDYLNKHLKSVKKIPSRGD (SEQ ID NO:11)  
RGDLSKSVKKIPSDFEGSGYTDLQE (SEQ ID NO:12)  
DSQAQKSPVKSSTHRIQHNIDYLNKHLKRGD (SEQ ID NO:13)  
RGDVKKIPSDFEGSGYTDLQE (SEQ ID NO:14)  
DSQAQKSPVKSSTHRIQHNIDYLNKRGD (SEQ ID NO:15)  
RGDIPSDFEGSGYTDLQE (SEQ ID NO:16)  
DSQAQKSPVKSSTHRIQHNIDRGD (SEQ ID NO:17)  
RGDDFEGSGYTDLQE (SEQ ID NO:18)  
DSQAQKSPVKSSTHRRGD (SEQ ID NO:19)  
RGDGSGYTDLQE (SEQ ID NO:20)  
DSQAQKSPVKRGD (SEQ ID NO:21)  
RGDGYTDLQE (SEQ ID NO:22)  
DSQAQKSRGD (SEQ ID NO:23)  
RGDNDISPFSGDGQPFKDIPGKGEATGPDLEGKDIQTGFA (SEQ ID NO:24)

Please amend the paragraph on page 11, beginning on line 17 (i.e., paragraph 0054) of the Substitute Specification as follows:

 Specific examples of the peptides of the invention which comprise the RGD internally include the following:

NDI **RGDSPFSGDGQPFKDIPGKGEATGPDLEGKDIQTGFA** (SEQ ID NO:25)  
NDISPF **RGDSGDGQPFKDIPGKGEATGPDLEGKDI** (SEQ ID NO:26)  
NDISPFSGD **RGDGQPFKDIPGKGEATGPD** (SEQ ID NO:27)  
FSGDGQPFKDIPGKGEATGPDLEGKDIQTGFAGPSEAES **RGDTHL** (SEQ ID NO:28)  
IPGKGEATGPDLEGKDIQTGFAGPSE **RGDAESTHL** (SEQ ID NO:29)  
EATGPDLEGKDIQTGFAG **RGDPSEAESTHL** (SEQ ID NO:30)  
NDISPFSGDGQPFKD **RGDIPGKGEATGPDLEGK** (SEQ ID NO:31)  
GKGEATGPDLEGKDI **RGDQTGFAGPSEAESTHL** (SEQ ID NO:32)  
FSGDGQPFKDIPGKGEATG **RGDPDLEGKDIQTGFAGPSEA** (SEQ ID NO:33)  
DGQPFKDIPGKGEATG **RGDPDLEGKDIQTGF** (SEQ ID NO:34)  
PFKDIPGKGEATG **RGDPDLEGKDIQ** (SEQ ID NO:35)  
DIPGKGEATG **RGDPDLEGKDIQTGFAGP** (SEQ ID NO:36)  
DGQPFKDIPGKGEATG **RGDPDLEGKDIQTGF** (SEQ ID NO:37)  
GKGEATG **RGDPDLEGKDIQTGFAGPSEA** (SEQ ID NO:38)  
EATG **RGDPDLEGKDIQTGF** (SEQ ID NO:39)  
EATG **RGDPDLEGK** (SEQ ID NO:40)  
EATG **RGDPDL** (SEQ ID NO:41)

Please amend the paragraph on page 14, beginning on line 15 (i.e., paragraph 0065) of the Substitute Specification, as follows:

 Six different peptides were manually synthesized by the 9-fluorenylmethoxycarbonyl (Fmoc) strategy and prepared in the C-terminal amide form. The six peptides are as follows:

D-00001: IPSDFEGSGYTDLQE (SEQ ID NO:42)  
D-00002: DFEGSGYTDLQERGD (SEQ ID NO:43)  
D-00003: YTDLQERGDNDISPF (SEQ ID NO:44)  
D-00004: ERGDNDISPFSGDGQ (SEQ ID NO:45)  
D-00005: NDISPFSGDGQPFD (SEQ ID NO:46)  
D-00006: TDLQERGDNDISPFSGDGQPFD (SEQ ID NO:47)

(C-terminus amidated)

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Please amend the paragraph on page 16, beginning on line 8 (i.e., paragraph 0071) of the Substitute Specification as follows:

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CE  
Conclude

The six peptides of Example 1 were tested for their ability to enhance bone growth with the tests being carried out as described above in Example 2. The peptides which did not include the RGD sequence did not show positive results. The other four peptides showed positive results with the best results being obtained with the sequences

D-00004: ERGDNDISPFSGDGQ (SEQ ID NO:45), and  
D-00006: TDLQERGDNDISPFSGDGQPFD (SEQ ID NO:47).

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